PERSPECTIVES

Mycotoxins and Disease:

A Critique of a Key But Scientifically Flawed Study

by Ronald E. Gots, M.D., Ph.D.

About the Author

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A study by Croft et al. entitled "Clinical Confirmation of Trichothecene Mycotoxicosis in Patient Urine," published in the July 2002 issue of *Journal of Environmental Biology*, appears, on its surface, to provide compelling scientific evidence of inhalational mycotoxin disease in individuals residing in contaminated residences.[1] It also strongly argues that urine tests for trichothecene mycotoxins **are** the new gold standard for assessing causation and linking symptoms or diseases to indoor environments. This extensive study, replete with citations, experimental elements, and far-reaching interpretations. is both dramatic and highly useful **far** plaintiff claims.

The problem is that this study is so replete with fundamental scientific and methodological errors that its conclusions range from speculation to sheer nonsense. This is **a** study which must be thoroughly understood by attorneys, plaintiff and defense, who deal with mold-related personal injury claims. A brief overview of this very important study and **a** more complete review of its fatal scientific flaws is provided here.

Dr. Croft, a veterinarian, is the lead author.[2] In his article on trichothecene mycotoxicosis' in patient urine, Croft describes in detail four cases of individuals, and hundreds of others, who were allegedly living in mold-contaminated environments and who purportedly fit the diagnosis of trichothecene mycotoxicosis. Using a variety of tests, including ***an*** unusual skin patch test, and urine extraction of alleged trichothecenes, he confirms exposure. Injecting rats with the urine extract produced similar disorders, further supporting his claims. A described autopsy of **a** deceased subject adds to the impact of his claims.

This paper appears to the non-scientist to be **a** careful, thorough study. Its conclusions seem strong and well-founded. Every disease and symptom from aneurysms to pancreatic and prostate cancer, through every one of at least fifty symptoms, are claimed to arise from trichothecene intoxication. Notwithstanding its peer-reviewed status and seeming validity, its flaws are so manifest that they will require careful dissection. A few key errors include:

- No controls;
- A **claim** of mycotoxin presence in the urine or the bloodstream without valid confirmation;
- The use of novel, ill-supported tests;
- Attribution of every imaginable symptom and disease to the alleged exposure, with no consideration of other, far more likely, alternate causes;
- Failure to consider normal dietary sources of trichothecenes;

There are many more. The paper is replete with overstatements, mischaracterizations, experimental design **flaws** and misuse of citations allegedly supporting the authors' methodologies. These points are sufficient to **call** into doubt all of the claims in this paper.

Having reviewed all of the articles cited by the authors, I shall summarize **a** few critical findings. The authors cite Ueno (1977, 1980, 1983) for their historical discussion of the manifestations of trichothecene mycotoxicosis. In none of Ueno's papers were the descriptions of illnesses comparable to those described by Croft. For example, in Ueno's 1977 paper,) specific illnesses associated with specific mycotoxins were described. The toxicological features of mycotoxin-induced illnesses **are** dependent upon the specific mycotoxin and the species of animal affected. Ueno characterized some of these distinctive disorders by their source, others by their clinical characteristics, e.g., B Alimentary toxic aleukia (ATA), moldy corn toxicosis, bean hull toxicosis, stachybotrytoxicosis and others.

Contrary to Croft's assertion, T-2 toxin is primarily eliminated via the GI tract and found in the feces. A smaller amount is found in the urine. The metabolic pathways by which mycotoxins are handled in the body vary among animal species. Since human metabolism is less well described than is animal, we are not currently in a position to make blanket statements about the metabolic process—that relate to T-2 toxin.

Croft asserts in his paper that certain urine extraction methods precipitate trichothecenes. This note is unreferenced and cannot be checked. Further, Croft claims that tests conducted on human urine indicate substantial corollaries to the same tests already observed using animal urine. This suggests that urinalysis confirms diagnoses in humans. These claims are not referenced, therefore, the methodology, which is certainly not a generally established practice, cannot be assessed or verified. Conclusions based on this methodology are neither valid nor reliable.

Croft attempts to use Koch's postulates,' the generally-accepted scientific standard for determining the presence of a pathogen and its cause of an illness, to establish that mycotoxicosis is caused by mold exposure. Croft's characterization of Koch's postulates, however, is entirely erroneous. Moreover, he does not adhere to any of them in his scientific investigations. These investigators have presented no objective, confirmatory data that they have extracted trichothecenes from these patients' urines, only conclusory statements. They state that "reproducing" the disease in animals proved that the trichothecenes were causal. However, we have no confirmation of trichothecene extraction. And, considering the generalized symptoms and "diseases" described in these patients, one wonders what is meant by "the disease."

In the patient discussions, exposures are never established, merely assumed. Temporal relationships between exposures and diseases varied from several months to twelve years. **Notably,** there is no mention of the diagnoses provided by treating physicians. This is particularly notable in Case 4, in which the pathologic features of a devastating encephalomyelopathy were identified. There are dozens of diseases known that cause this condition: mycotoxicosis is not one of them.

Croft erroneously cited a test and misused a skin patch test (Higuchi et al.) upon which Craft and his co-investigators relied heavily.^{5} The patch test for "alcohol dehydrogenase" supposedly measured an enzyme affected by mycotoxins. First, there is no established basis for the assumption that mycotoxins affect alcohol dehydrogenase. Second, the Higuchi letter (it is a Letter-to-an-Editor, not a peer-reviewed study) was designed to test Asians, a significant proportion of whom have an inherited deficiency in aldehyde (not alcohol, as Croft stated) dehydrogenase, making them intolerant to alcohol. Croft somehow assumed that a positive test in their subjects reflected mycotoxin effect, an effect which is medically unknown. Even assuming that this skin test was positive (Croft got the enzyme wrong), it could well have suggested an inherited defect as noted by the authors they cited.

Finally, Croft went far beyond the test protocol of the cited author. Croft and his co-authors used a different method and a different scoring system, protocols which have not been validated. Nevertheless, they use this test extensively, suggesting that it quantified the extent of toxicity: a misleading, unwarranted suggestion.

Another important component of Croft's study involved the alleged extraction of trichothecenes from urine. He and his co-authors give no references for their method and there is little reason to believe that trichothecenes were extracted. Their conclusory statement that this was tested by thin layer chromatography (TLC) is not properly discussed. They state that their TLC results were consistent with those reported for trichothecenes, but which of the trichothecenes? Each trichothecene comes out at a different place on TLC.

SPECT scans were used to demonstrate "neurotoxicity" by these authors, yet such scans have little value for that purpose." A consensus document' and review articles by The Society of Nuclear Medicine Brain Imaging Council have addressed the issue that SPECT scans have little value for demonstrating neurotoxicity. In fact, SPECT scans presented by the consultant used in this Croft paper have been excluded in court proceedings as being misleading.

The authors invoke other non-standard tests for mycotoxin presence in urine. For example, they state that urine samples left at room temperature for five months showed no 'putrefaction" and excessive protein at the bottom of the container. How and why these constitute measures of the presence of mycotoxins is merely stated with no support and no logical basis.

Even assuming that the authors were finding mycotoxins, the study is fatally flawed by lack of controls. Croft states that one of the authors was the control, but since he entered the subject homes and felt ill, how could he have been a control? He was exposed to the environment and had a response similar to that of the other study subjects. Furthermore, a single control, and no blinding, is inappropriate. Even if trichothecenes had actually been found, we eat them everyday in foodstuffs. How does the author know what background or "normal" levels are?

Finally, the sheer range of symptoms, as well as the presence of actual serious and even fatal diseases, described in this article are a veritable compendium of all human ailments. It would have been quite helpful if the authors had provided more information about standard diagnostic testing and diagnoses made by various treating physicians.

Endnotes

1. The full reference is: Croft WA, Jastromski BM, Croft AL, Peters HA. Clinical Confirmation of Tricothecene Mycotoxicosis in Patient Urine. *Journal of Environmental Biology* 2002;23(3) 301-20. To read the article abstract, visit PubMed Online (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) and enter the PMID number 12597576.

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